EPA Human Studies Review Board (HSRB)

July 25, 2018 Meeting Minutes

Committee Members: (See EPA HSRB Members List – Attachment A)

Date and Time: Wednesday, July 25, 2018, 1:00 to 5:30 pm EST.

Locations: Via teleconference and webinar

Purpose: The HSRB provides advice, information and recommendations on issues related to scientific and ethical aspects of human subjects research.

Meeting was called to order at 1:00 p.m.by Tom O'Farrell, designated federal official (DFO) for the HSRB. Roll was taken and the following members and observers were present:

HSRB members	EPA staff members
Edward Gbur, Jr., Ph.D. (HSRB Vice-Chair) Jennifer Cavallari, Sc.D., CIH Alesia Ferguson, Ph.D. Kyle L. Galbraith, Ph.D. Walter T. Klimecki, D.V.M., Ph.D. Randy Maddalena, Ph.D. Jun Zhu, Ph.D. Kendra Lawrence, Ph.D., consultant	Michelle Arling (EPA, OPP) Helen Hull-Sanders (EPA, OPP) Matt Aubuchon (EPA, OPP) Jennifer Saunders (EPA, OPP) Anna Briley (EPA, OPP) Tom O'Farrell (OSA)
Members of the public, representatives of research sponsor and research team Tim Blatchford (Pulcra Chemicals) Luther Dasher (Pulcra Chemicals) Carey Griffon (Pulcra Chemicals) Jeff Carr (Pulcra Chemicals) Kristine Styer (i2LResearch) Timothy Foard (i2LResearch) Albert Allen (Eli Lilly) Lisa Corey (Intertox) Lindsay McNair (WIRB-Copernicus Group) Kurd Ali (EnDyna) Kevin Dunn (EnDyna)	

Tom O'Farrell provided an introduction to the meeting and outlined the Federal Advisory Committee Act (FACA) procedures. Ms. Michelle Arling said that EPA is working on issuing a proposed rule to harmonize Subpart K with the revisions to the Common Rule. EPA plans to have the EPA harmonized rule finalized by early 2019, to align with the compliance date for the revised Common Rule. The proposed rule will be submitted to OMB and public comment. The HSRB will be able to review it as well.

The Board reviewed one protocol during the session on July 25, 2018, "Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings". The Agency's scientific review of this protocol was presented by Helen Hull-Sanders of the EPA Office of Pesticide Programs (OPP). The study protocol was submitted by i2L Research on behalf of Pulcra and it is designed to assess the bite protection performance of military fabrics. The study tests the hypothesis that clothing treated with permethrin will increase mosquito bite protection. A subject's arm will be exposed to mosquitoes for 15 minutes for each fabric treatment of 0, 50, 75, and 100 washes. After each 15 minute interval, all mosquitoes will be removed from the cage and crushed to determine if they had a blood meal. Two types of military fabrics will be tested. It was determined that the maximum amount of permethrin subjects could receive, 3.6 mg per day, is well below the Agency's level of concern. EPA recommended the protocol to be revised to include a description of the types of fabrics to be tested. EPA also recommended that the sponsor include information on how bite-through protection will be determined and specific details about the fabrics when they are tested. EPA also recommended that the protocol be revised to include a description of the drying cycle, both after the chemical padding process and between washes. EPA also recommended that i2L Research describe how they will analyze the fabrics at each washing interval for permethrin retention and describe in detail the sequence of tests for each arm over the full course of the test day. Finally, EPA recommended that i2L Research provide some clarifying details about the sleeve construction and attachment during the tests and describe any and all technicians' duties during the test day related to interaction with the human subjects.

The Board then asked questions about the science presentation. Dr. Walt Klimecki had a concern that there might be considerable variability in the amount of permethrin loaded on the fabrics. Dr. Helen Hull-Sanders responded that it is EPA's understanding that it will be controlled at 0.52%. Dr. Randy Maddalena asked if this is just a specific protocol for this permethrin treatment on these listed fabrics in the protocol. Ms. Arling responded that this protocol is for testing permethrin-treated fabrics and that the plan is to test flame-resistant Army combat uniform or a similar fabric, an Army combat uniform or something similar in terms of weave, and then some representative consumer fabric.

Ms. Arling of EPA OPP reviewed the ethical aspects of the study protocol. This research is needed because existing data are not sufficient to support registration of these treated fabrics. Human subjects must be used because there are no non-human testing options that would provide the necessary data. Those interested candidates who pass the preliminary screening via the website and who are qualified, will be contacted by a member of the study team to establish basic qualification for the study. A second conversation will include a more detailed description of the study and a screening of the interested person against a subset of the eligibility criteria. EPA included specific recommendations for revising the protocol, including clarifying which treatment method, such as padding, will be used for the fabrics used in the study. EPA also recommended that the protocol be revised to delete the statement that each test substance will be evaluated by the IRB prior to testing, and to ensure that the language about the IRB is consistent. The overseeing IRB who approves the protocol is Schulman, which has since merged with Advarra, and the protocol should reflect this updated IRB oversight when the transition has been completed. In addition, EPA recommended revising the protocol to include specific language that IRB approval will be obtained before implementing any amendments and that deviations will be reported promptly. EPA determined that the protocol includes measures demonstrating respect for subjects. It is noted that Schulman is merging with another IRB to form Advarra IRB. Depending on the schedule for review and approval of the final protocol, either Schulman or Advarra will issue the approval and

conduct oversight of the research. EPA determined that there were no deficiencies relative to EPA's human studies Rule 40 CFR Part 26, Subparts K and L, or to FIFRA, provided the study sponsor implements all recommendations from EPA, the IRB, and the HSRB.

The Board then asked questions about the Ethics Review. Dr. Kyle Galbraith asked whether it will be verified that only non-nursing women will be entered in the study. Ms. Arling responded that nursing women will be screened out by a question. Dr. Ed Gbur asked why there is an upper limit of 55 years old for subjects. Ms. Arling responded that there is no objection to this age limit but EPA is verifying the rationale for it.

Tom O'Farrell then read a statement from William Jordan from the public.

The HSRB's scientific review was presented by Board members Drs. Walt Klimecki and Randy Maddalena and consultant Dr. Kendra Lawrence. Dr. Walt Klimecki stated that he had no great concerns from a toxicology standpoint. However, Dr. Klimecki stated that he was not sure how they are going to control that all fabrics were going to contain the same amount of permethrin. Dr. Randy Maddalena also had the same question about loading permethrin onto the fabric. Mr. Luther Dasher (Pulcra) responded that permethrin will be applied by a pad and that the amount of permethrin loaded onto the fabric will be measured analytically. Dr. Maddalena asked why washing studies would continue down to zero if a higher washing number satisfied the objective of 90% protection. Dr. Kendra Lawrence asked whether DOD is part of the approval process for this protocol. Dr. Lawrence also asked if there was any value in confirming that the mosquitoes used were disease free since they are already documented to be disease free from the supplier. The Board decided unanimously that the protocol is likely to generate scientifically reliable data used for estimating the level of mosquito bite protection provided by the different textiles treated with permethrin if the recommendations from the EPA and the HSRB are included.

Dr. Kyle Galbraith presented the HSRB's ethics review of the study. Dr. Galbraith questioned the 55 year old age limit for study participants. Dr. Galbraith suggested that it be made clear to participants early on that the mosquitoes used will not carry diseases.

The Board voted unanimously that pending clarification of the procedures involved in the preliminary attractiveness study, justification or removal of the age limit, and then with the clarifications requested by EPA and the HSRB in the science and ethics reviews, that the research is likely to meet the applicable requirements of 40 CFR, part 26, sub-parts K and L.

The HSRB recommends the following edits to the protocol:

- All edits outlined in the EPA's science and ethics review of the protocol should be incorporated.
- More explicit details should be included in the protocol on how the amount of permethrin initially loaded onto the fabric will be determined and how the residue will be measured.
- Include justification in the protocol for starting with the 100 washing level test rather than randomizing the order of the washing level tests.
- Include justification in the protocol as to why starting with the 100 washing level test does not eliminate the need for testing at fewer washing levels.

- The age limit for participation should be justified or removed from the protocol.

- Clarification and additional information on the attractiveness phase should be provided in the protocol regarding whether a subject's arm will be exposed to mosquitos or whether there will be a physical barrier between the mosquitos and the subject's arm.
- The protocol should make it clear during the participant screenings that the mosquitoes used in the tests have been certified as disease free.
- A rationale for the participant's health insurance to be the primary provider of coverage should an injury occur during the test should be included in the protocol.

This concluded the Board's session for July 25, 2018 and the meeting was adjourned.

Respectfully submitted:

Thomas J. O'Farrell, 10/9/18

Thomas O'Farrell
Designated Federal Officer
Human Studies Review Board
United States Environmental Protection Agency

Certified to be true by:

Edward E Gbur, Jr 10/10/2018

Ed Gbur, Ph.D.
Co-Chair
Human Studies Review Board
United States Environmental Protection Agency

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by Board members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect definitive consensus advice from the Board members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final report prepared and transmitted to the EPA Science Advisor following the public meeting.

Attachment A
EPA HUMAN STUDIES REVIEW BOARD MEMBERS

Chair

Liza Dawson, Ph.D.
Research Ethics Team Leader
Division of AIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

Vice Chair

Edward Gbur, Jr., Ph.D.
Professor of Statistics
Director, Agricultural Statistics Laboratory
University of Arkansas
Fayetteville, AR

Members

Jennifer Cavallari, Sc.D., CIH
Assistant Professor
Division of Occupational and Environmental Medicine
University of Connecticut
Storrs, CT

Alesia Ferguson, Ph.D.
Associate Professor
Department of Environmental and Occupational Health
University of Arkansas
Little Rock, AR

Kyle L. Galbraith, Ph.D.
Human Subjects Protection
Carle Foundation Hospital
Urbana, IL

Walter T. Klimecki, D.V.M., Ph.D.
Associate Professor
Departments of Pharmacology and Toxicology
The University of Arizona Health Sciences
Tucson, AZ

Randy Maddalena, Ph.D.
Physical Research Scientist
Indoor Environment Group
Lawrence Berkeley National Laboratory
Berkeley, CA

Jun Zhu, Ph.D.
Professor of Statistics and of Entomology
Department of Statistics
University of Wisconsin–Madison
Madison, WI

Consultants to the Board

Kendra L. Lawrence, Ph.D., BCE, PMP
Health Sciences Product Manager
U.S. Army Medical Materiel Development Activity
Fort Detrick, MD

Attachment B
Federal Registers Notice Announcing Meetings

ENVIRONMENTAL PROTECTION AGENCY

[FRL-9980-61-ORD]

Human Studies Review Board; Notification of Public Meetings

AGENCY: Environmental Protection Agency.

ACTION: Notice.

SUMMARY: The Environmental Protection Agency (EPA), Office of the Science Advisor announces two separate public meetings of the Human Studies Review Board (HSRB) to advise the Agency on the ethical and scientific review of research involving human subjects.

DATES: A virtual public meeting will be held on Wednesday, July 25, 2018, from 1:00 pm to approximately 5:30 pm Eastern Time. A separate, subsequent teleconference meeting is planned for Thursday, September 13th, 2018, from 2:00 pm to approximately 3:30 pm Eastern Time for the HSRB to finalize its Final Report of the July 25, 2018 meeting and review other possible topics.

ADDRESSES: All of these meetings will be conducted entirely by telephone and on the Internet using Adobe Connect. For detailed access information visit the HSRB Website: http://www2.epa.gov/osa/human-studies-review-board

FOR FURTHER INFORMATION, CONTACT: Any member of the public who wishes to receive further information should contact the HSRB Designated Federal Official (DFO),

Thomas O'Farrell on telephone number (202) 564-8451; fax number: (202) 564-2070; email address: ofarrell.thomas@epa.gov; or mailing address: Environmental Protection Agency, Office of the Science Advisor, Mail code 8105R, 1200 Pennsylvania Avenue NW, Washington, DC 20460.

SUPPLEMENTARY INFORMATION:

Meeting access: These meetings will be open to the public. The full Agenda and meeting materials will be available at the HSRB Website: http://www2.epa.gov/osa/human-studies-review-board . For questions on document availability, or if you do not have access to the Internet, consult with the DFO, Thomas O'Farrell, listed under FOR FURTHER INFORMATION, CONTACT.

Special accommodations. For information on access or services for individuals with disabilities, or to request accommodation of a disability, please contact the DFO listed under FOR FURTHER INFORMATION, CONTACT at least 10 days prior to the meeting to give EPA as much time as possible to process your request.

How May I Participate in this Meeting?

The HSRB encourages the public's input. You may participate in these meetings by following the instructions in this section.

1. Oral comments. To pre-register to make oral comments, please contact the DFO, Thomas O'Farrell, listed under FOR FURTHER INFORMATION, CONTACT. Requests to present oral comments during the meeting will be accepted up to Noon Eastern Time on

Wednesday, July 18, 2018, for the July 25, 2018 meeting and up to Noon Eastern Time on Thursday, September 6, 2018 for the September 13, 2018 meeting. To the extent that time permits, interested persons who have not pre-registered may be permitted by the HSRB Chair to present oral comments during either meeting at the designated time on the agenda. Oral comments before the HSRB are generally limited to five minutes per individual or organization. If additional time is available, further public comments may be possible.

2. Written comments. Submit your written comments prior to the meetings. For the Board to have the best opportunity to review and consider your comments as it deliberates, you should submit your comments by Noon Eastern Time on Wednesday, July 18, 2018, for the July 25, 2018 meeting and up to Noon Eastern Time on Thursday, September 6, 2018 for the September 13, 2018 meeting. If you submit comments after these dates, those comments will be provided to the HSRB members, but you should recognize that the HSRB members may not have adequate time to consider your comments prior to their discussion. You should submit your comments to the DFO, Thomas O'Farrell listed under FOR FURTHER INFORMATION, CONTACT**.** There is no limit on the length of written comments for consideration by the HSRB.

Background

The HSRB is a Federal advisory committee operating in accordance with the Federal Advisory Committee Act 5 U.S.C. App.2 § 9. The HSRB provides advice, information, and recommendations on issues related to scientific and ethical aspects of third-party human subjects research that are submitted to the Office of Pesticide Programs (OPP) to be used for regulatory purposes.

Topic for discussion. On July 25, 2018, EPA's Human Studies Review Board will consider a study protocol titled "Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings" submitted by Pulcra Industries.

The Agenda and meeting materials for this topic will be available in advance of the meeting at http://www2.epa.gov/osa/human-studies-review-board.

On September 13, 2018, the HSRB will review and finalize their draft Final Report from the July 25, 2018 meeting, in addition to other topics that may come before the Board. The HSRB may also discuss planning for future HSRB meetings. The agenda and the draft report will be available prior to the meeting at http://www2.epa.gov/osa/human-studies-review-board.

Meeting minutes and final reports. Minutes of these meetings, summarizing the matters discussed and recommendations made by the HSRB, will be released within 90 calendar days of the meeting. These minutes will be available at http://www2.epa.gov/osa/human-studies-review-board. In addition, information regarding the HSRB's Final Report, will be found at http://www2.epa.gov/osa/human-studies-review-board or from Thomas O'Farrell listed under FOR FURTHER INFORMATION, CONTACT.

Date: _____

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Jennifer Orme-Zavaleta, Ph.D.
EPA Science Advisor